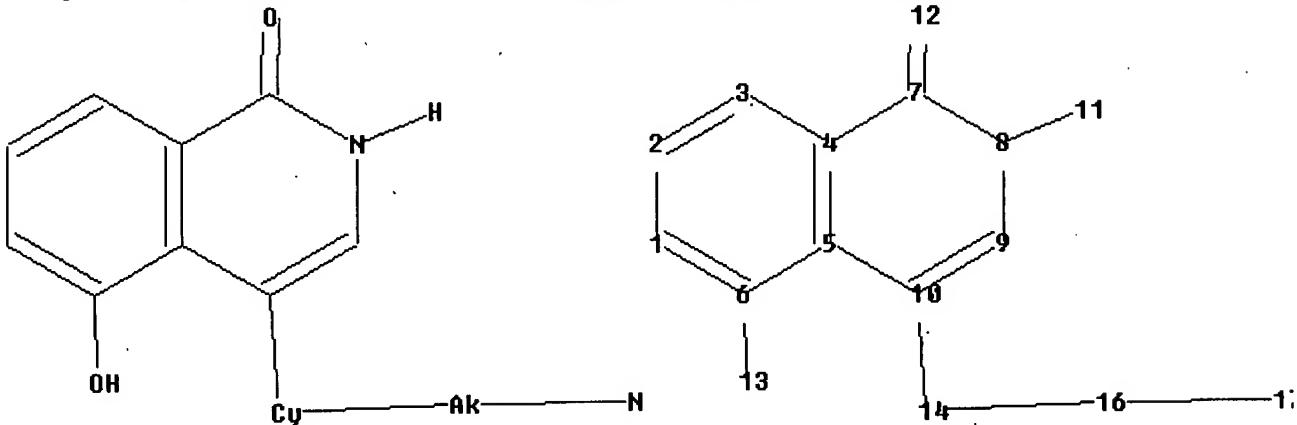


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* STN Columbus * * * * * * * * * * * * *

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chain nodes :
11 12 13 14 16
ring nodes :
1 2 3 4 5 6 7 8 9 10
ring/chain nodes :
17
chain bonds :
6-13 7-12 8-11 10-14 14-16 16-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10
exact/norm bonds :
4-7 5-10 6-13 7-8 7-12 8-9 9-10 10-14 14-16 16-17
exact bonds :
8-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:Atom 16:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> s 11 sam
L2 1 SEA SSS SAM L1

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L3 144 SEA SSS FUL L1

=> file caplus

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22724470 PD< JULY 2002

(PD<20020700)

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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1137938 CAPLUS Full-text

DN 144:45339

TI Neuroprotective effects of KCL-440, a new poly(ADP-ribose) polymerase inhibitor, in the rat middle cerebral artery occlusion model

AU Ikeda, Yasuhiko; Hokamura, Kazuya; Kawai, Tomoyuki; Ishiyama, Junichi; Ishikawa, Kumi; Anraku, Tsuyoshi; Uno, Takashi; Umemura, Kazuo

CS Department of Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, 432-8014, Japan

SO Brain Research (2005), 1060(1-2), 73-80

CODEN: BRREAP; ISSN: 0006-8993

PB Elsevier B.V.

DT Journal

LA English

AB It is reported that ischemic brain injury is mediated by the activation of poly(ADP-ribose) polymerase (PARP). In this study, we examined the pharmacological profile of KCL-440, a new PARP inhibitor, and its neuroprotective effects in the rat acute cerebral infarction model induced by photothrombotic middle cerebral artery (MCA) occlusion. In an *in vitro* study, KCL-440 exhibited potency with regard to inhibition of PARP activity, with an IC₅₀ value of 68 nM. An *in vivo* pharmacokinetic study showed that the brain concentration of KCL-440 was sufficient to inhibit PARP activity during the *i.v.* infusion of KCL-440 at the rate of 1 mg/kg/h. KCL-440 at various doses or saline was administered for 24 h immediately after the MCA occlusion. Administration of KCL-440 led to a dose-dependent reduction in the infarct size at 24 h after MCA occlusion. Infarct sizes were 44.8% ± 3.0% (n = 8), 40.5% ± 1.1% (n = 8), 38.2% ± 1.4% (n = 8), 35.1% ± 2.1% (n = 8), 34.2% ± 2.3% (n = 7), 32.6% ± 1.9% (n = 8), and 31.0% ± 2.1% (n = 5) at doses of 0, 0.01, 0.03, 0.1, 0.3, 1.0, and 3.0 mg/kg/h. When compared to the control group, a statistically significant difference was observed in the doses that were higher than 0.03 mg/kg/h. When the infusion of KCL-440 (1 mg/kg/h, n = 8) was started at 1 h after the MCA occlusion, a significant reduction in infarct size was observed; this was not observed when KCL-440 infusion was started 2 or 3 h after the MCA occlusion. Furthermore, increased poly(ADP-ribose) immunostaining was confirmed at the ischemic border zone 2 h after the MCA occlusion, and it was reduced by KCL-440 treatment. These results suggest that KCL-440 is a possible neuroprotective agent with high blood-brain barrier permeability and high PARP inhibitory activity.

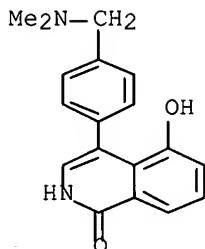
IT 651029-09-3, KCL 440

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuroprotective effects of KCL-440, a new poly(ADP-ribose) polymerase inhibitor, in the rat middle cerebral artery occlusion model)

RN 651029-09-3 CAPLUS

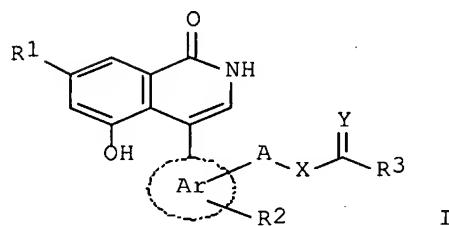
CN 1(2H)-Isoquinolinone, 4-[4-[(dimethylamino)methyl]phenyl]-5-hydroxy- (CA INDEX NAME)



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2004:252487 CAPLUS Full-text
 DN 140:287279
 TI Preparation of 4-(substituted aryl)-5-hydroxyisoquinolinone derivatives as poly(ADP-ribose) polymerase inhibitors
 IN Shiga, Futoshi; Kanda, Takahiro; Takano, Yasuo; Ishiyama, Junichi
 PA Kyorin Pharmaceutical Co., Ltd., Japan
 SO PCT Int. Appl., 134 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004024694 | A1 | 20040325 | WO 2003-JP11346 | 20030905 |
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2003264386 | A1 | 20040430 | AU 2003-264386 | 20030905 |
| PRAI | JP 2002-263918 | A | 20020910 | | |
| | WO 2003-JP11346 | W | 20030905 | | |
| OS | MARPAT 140:287279 | | | | |
| GI | | | | | |



AB Title compds. I (R1 = H, halo; R2 = H, halo, OH, alkyl, haloalkyl, alkoxy, haloalkoxy; Ar = Ph, naphthyl, heteroaryl, etc.; A = bond, alkylene; X = bond, O, amino; Y = O, S; R3 = amino, etc) and their pharmacol. acceptable salts, useful as poly(ADP-ribose) polymerase inhibitors, are prepared 1,2-Dihydro-5-hydroxy-4-[4-(N-methylcarbamoyl)phenyl]-1-oxoisouinoline was prepared and showed inhibitory activity against PARP with IC50 of 144 n mol/L.

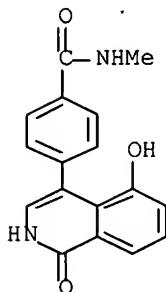
IT 675577-26-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-(substituted aryl)-5-hydroxyisoquinolinone derivs. as poly(ADP-ribose) polymerase inhibitors)

RN 675577-26-1 CAPLUS

CN Benzamide, 4-(1,2-dihydro-5-hydroxy-1-oxo-4-isouinolinyl)-N-methyl- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:80658 CAPLUS Full-text

DN 140:146017

TI Preparation of hydroxyisoquinolinone derivatives as poly(ADP-ribose) polymerase inhibitors

IN Shiga, Futoshi; Kanda, Takahiro; Kimura, Tetsuya; Takano, Yasuo; Ishiyama, Junichi; Kawai, Tomoyuki; Anraku, Tsuyoshi; Ishikawa, Kumi

PA Kyorin Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 151 pp.

CODEN: PIXXD2

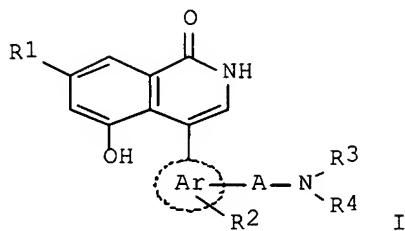
DT Patent

LA Japanese

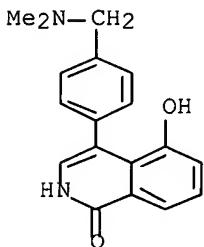
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2004009556 | A1 | 20040129 | WO 2003-JP9332 | 20030723 |
| | WO 2004009556 | A9 | 20041021 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, | | | |

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2493234 A1 20040129 CA 2003-2493234 20030723
 AU 2003255149 A1 20040209 AU 2003-255149 20030723
 EP 1544194 A1 20050622 EP 2003-765364 20030723
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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 CN 1671668 A 20050921 CN 2003-817589 20030723
 NZ 537793 A 20070531 NZ 2003-537793 20030723
 US 2006173039 A1 20060803 US 2005-521565 20050119
 MX 2005PA00983 A 20050818 MX 2005-PA983 20050124
 PRAI JP 2002-214673 A 20020724
 WO 2003-JP9332 W 20030723
 OS MARPAT 140:146017
 GI



AB Title compds. I (ring Ar = Ph, naphthyl, 5- or 6-membered heteroaryl, R1 = H, halo; R2 = H, halo, OH, alkyl, aryl, etc.; R3, R4 = H, halo, etc; A = alkylene, alkenylene) and their pharmacol. acceptable salts, useful as poly(ADP-ribose) polymerase (PARP) inhibitors, are prepared. Thus, 1,2-dihydro-4-[4-(dimethylaminomethyl)phenyl]-5-hydroxy-1-oxoisoquinoline was prepared and showed inhibition of PARP with IC50 of 30 nM.
 IT 651029-09-3P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of hydroxyisoquinolinone derivs. as poly(ADP-ribose) polymerase inhibitors)
 RN 651029-09-3 CAPLUS
 CN 1(2H)-Isoquinolinone, 4-[4-[(dimethylamino)methyl]phenyl]-5-hydroxy- (CA INDEX NAME)



10/521,565

ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN INTERNATIONAL LOGOFF AT 17:05:14 ON 08 NOV 2007